Coarse powder Not less than 95% by weight passes through a number 1400 sieve and not more than 40% by weight passes through a number 355 sieve.

Moderately fine powder Not less than 95% by weight passes through a number 355 sieve and not more than 40% by weight passes through a number 180 sieve.

Fine powder Not less than 95% by weight passes through a number 180 sieve and not more than 40% by weight passes through a number 125 sieve.

Very fine powder Not less than 95% by weight passes through a number 125 sieve and not more than 40% by weight passes through a number 90 sieve.

Within the monographs of the British Pharmacopoeia the following terms may be used in addition to those defined above, which are those of the European Pharmacopoeia. They are usually used to specify the degree of coarseness or fineness of a medicinal or pharmaceutical substance in powder form that is to be incorporated into a formulated preparation.

When the use of sieves is inappropriate, the definition is expressed in terms of the particle size as determined by suitable microscopical examination.

Moderately coarse powder Not less than 95% by weight passes through a number 710 sieve and not more than 40% by weight passes through a number 250 sieve.

Microfine powder Not less than 90% by weight of the particles passes through a number 45 sieve.

Superfine powder Not less than 90% by number of the particles are less than 10 µm in size.

C. Pressurised Inhalations: Deposition of the Emitted Dose

Replace by the following.

C1. Preparations for Inhalation: Aerodynamic Assessment of Fine Particles

This test is used to determine the fine particles fraction in the aerosols generated by preparations for inhalation.

Unless otherwise justified and authorised, one of the following apparatus and test procedures is used.

Apparatus A (Glass Impinger)

The apparatus is shown in Fig. 60 (see also Table I).

Procedure for nebulisers

Introduce 7 ml and 30 ml of a suitable solvent into the upper and lower impingement chambers, respectively.

Connect all the component parts, ensure that the assembly is vertical and adequately supported and that the jet spacer peg of the lower jet assembly just touches the bottom of the lower impingement chamber. Connect a suitable pump fitted with a filter (of suitable pore size) to the outlet of the apparatus and adjust the airflow through the apparatus, as measured at the inlet to the throat, to 60±5 litres per minute.

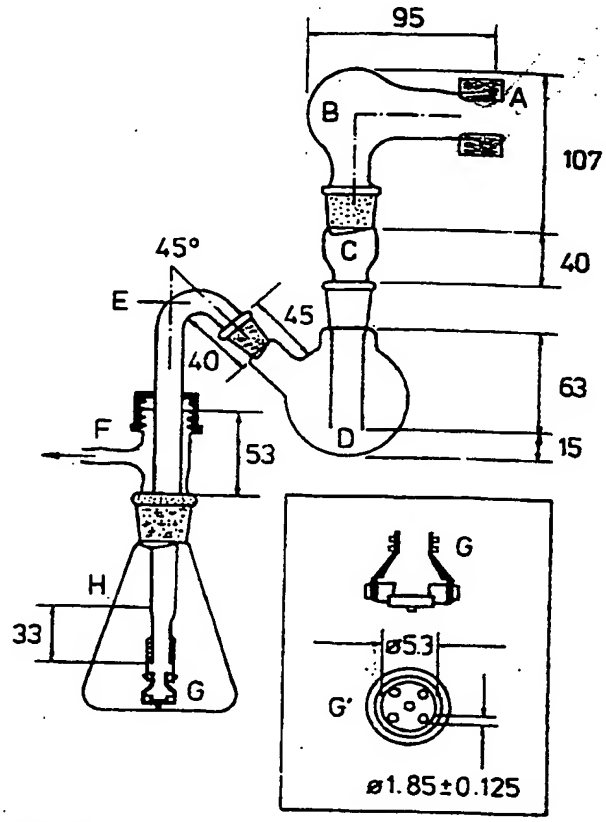

Fig. 60
Apparatus A for the aerodynamic assessment of fine particles
Dimensions in mm

Introduce the liquid preparation for inhalation into the reservoir of the nebuliser. Fit the mouthpiece and connect it by means of an adaptor to the device.

Switch on the pump of the apparatus and after 10 seconds switch on the nebuliser.

After 60 seconds, unless otherwise justified, switch off the nebuliser, wait for about 5 seconds and then switch off the pump of the apparatus. Dismantle the apparatus and wash the inner surface of the upper impingement chamber collecting the washings in a volumetric flask. Wash the inner surface of the lower impingement chamber collecting the washings in a second volumetric flask. Finally, wash the filter preceding the pump and its connections to the lower impingement chamber and combine the washings with those obtained from the lower impingement chamber. Determine the amount of active ingredient collected in each of the two flasks. Express the results for each of the two parts of the apparatus as a percentage of the total amount of active ingredient.

Procedure for pressurised inhalers

Place the actuator adaptor in position at the end of the throat so that the mouthpiece end of the actuator, when inserted to a depth of about 10 mm, lines up along the horizontal axis of the throat and the open end of the actuator, which accepts the pressurised container, is

uppermost and in the same vertical plane as the rest of the apparatus.

Introduce 7 ml and 30 ml of a suitable solvent into the upper and lower impingement chambers, respectively.

Connect all the component parts and ensure that the assembly is vertical and adequately supported and that the lower jet-spacer peg of the lower jet assembly just touches the bottom of the lower impingement chamber. Connect a suitable pump to the outlet of the apparatus and adjust the air flow through the apparatus, as measured at the inlet to the throat, to 60 ± 5 litres per minute.

Prime the metering valve by shaking for 5 seconds and discharging once to waste; after not less than 5 seconds, shake and discharge again to waste. Repeat a further three times.

Shake for about 5 seconds, switch on the pump to the apparatus and locate the mouthpiece end of the actuator in the adaptor, discharge once immediately. Remove the assembled inhaler from the adaptor, shake for not less than 5 seconds, relocate the mouthpiece end of the actuator for a further eight times, shaking between actuations. After discharging the tenth delivery, wait for not less than 5 seconds and then switch off the pump. Dismantle the apparatus.

Wash the inner surface of the inlet tube to the lower impingement chamber and its outer surface that projects

TABLE I Details of Apparatus A

Item	Description	Identifying Code[1]	Dimensions[2] mm
Mouthpiece adapter	Moulded rubber adapter for actuator mouthpiece	A	
Throat	Modified round-bottomed flask	B	50 ml
	ground-glass inlet socket		29/32
	ground-glass outlet cone		24/29
Neck	Modified glass adaptor	C	
	ground-glass inlet socket		24/29
	ground-glass outlet cone		24/29
	Lower outlet section of precision-bore glass tubing		
	bore diameter		14
	Selected-bore light-wall glass tubing		
	external diameter		17
Upper impingement chamber	Modified round-bottomed flask	D	100 ml
	ground-glass inlet socket		24/29
	ground-glass outlet cone		24/29
Coupling tube	Medium wall glass tubing	E	
	ground-glass cone		14/23
	Bent section and upper vertical section		
	external diameter		13
	Lower vertical section		
	external diameter		8
Screwthread, side-arm adapter	Plastic screw cap	F	28/13
	Silicone rubber ring		28/11
	PTFE washer		28/11
	Glass screwhead, *threadsize*		28
	Side-arm outlet to vacuum pump,		
	minimum bore diameter		5
Lower jet assembly	Modified polypropylene[3] filter holder connected to lower vertical section of coupling tube by PTFE tubing	G	See Fig. 60
	Acetal circular disc with the centres of four jets arranged on a projected circle of diameter 5.3 mm with an integral jet spacer peg	G'	10
	peg diameter		2
	peg protrusion		2
Lower impingement chamber	Conical flask	H	250 ml
	ground-glass inlet socket		24/29

[1]On Fig. 60

[2]Dimensions of ground-glass sockets and cones are specified in terms of the ISO designation in accordance with British Standard 572:1960. Quickfit apparatus is suitable.

[3]A modified Millipore Swinnex 13 polypropylene filter holder is suitable.

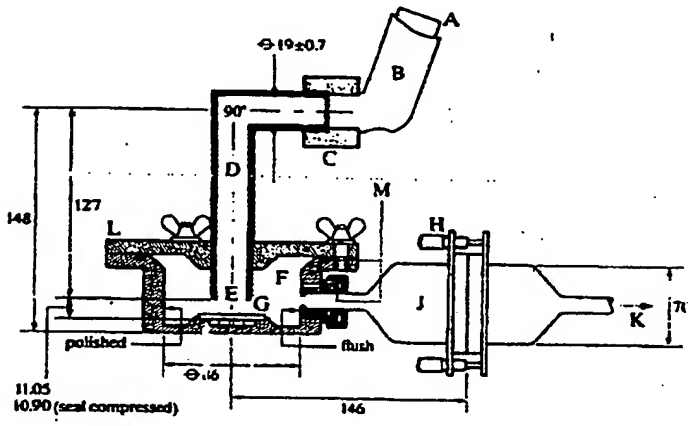

Fig. 61a
Apparatus B for the aerodynamic assessment of fine particles
Dimensions in mm

A— Pressurised inhalation container
B— Actuator
C— Adaptor
D— Throat
E— Jet
F— Impingement chamber
G— Sintered-glass disc (BS porosity No. 1)
H— Stainless steel filter clamp
J— Glass filter assembly
K— Vacuum Pump
L— Aluminium impingement chamber pump
M— Rubber O-rings

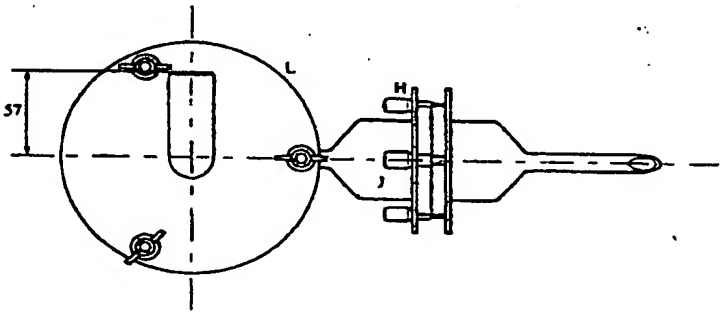

Fig. 61b
Apparatus B for the aerodynamic assessment of fine particles (top elevation)
Dimensions in mm

into the chamber with a suitable solvent collecting the washings in the lower impingement chamber. Determine the content of active ingredient in this solution. Calculate the amount of active ingredient collected in the lower impingement chamber per actuation of the valve and express the results as a percentage of the dose stated on the label.

Procedure for powder inhalers

Introduce 7 ml and 30 ml of a suitable solvent into the upper and lower impingement chambers, respectively.

Connect all the component parts and ensure that the assembly is vertical and adequately supported and that the jet spacer peg of the lower jet assembly just touches the bottom of the lower impingement chamber. Without the inhaler in place, connect a suitable pump to the outlet of the apparatus and adjust the air flow through the apparatus, as measured at the inlet to the throat, to 60±5 litres per minute.

Prepare the inhaler for use and locate the mouthpiece in the apparatus by means of a suitable adaptor. Switch on the pump for 5 seconds. Switch off the pump and remove the inhaler. Repeat for a further nine discharges. Dismantle the apparatus.

Wash the inner surface of the inlet tube to the lower impingement chamber and its outer surface that projects into the chamber with a suitable solvent, collecting the washings in the lower impingement chamber. Determine the content of active ingredient in this solution. Calculate the amount of active ingredient collected in the lower impingement chamber per discharge and express the results as a percentage of the dose stated on the label.